

CLAIMS

What is claimed is:

1. An isolated polynucleotide, wherein the polypeptide comprises a sequence of amino acid residues that is selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);

(e) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);

(f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val);

(g) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile);

(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 732 (Val); and

(i) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 1 (Met) to amino acid number 649 (Ile).

2. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 851;

(b) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 1727;

(c) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 1799;

(d) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 1800 to amino acid number 2366;

(e) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 1791 to amino acid number 2108;

(f) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 2366;

(g) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 219 to amino acid number 2108;

(h) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 171 to amino acid number 2366;

(i) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 162 to amino acid number 2108; and

(j) a polynucleotide sequence complementary to (a) through (i).

3. An isolated polynucleotide according to claim 1, wherein the polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

4. An isolated polynucleotide according to claim 1, wherein the polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2 or 544 (Lys) to 649 (Ile) of SEQ ID NO:46.

5. An isolated polynucleotide according to claim 1, wherein the polypeptide encoded by the polynucleotide has activity as measured by cell proliferation, activation of transcription of a reporter gene, or wherein the polypeptide encoded by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids from the group consisting of:

(a) the polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ ID NO:2;

(b) the polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ ID NO:2;

(c) the polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ ID NO:2;

(d) the polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ ID NO:2;

(e) the polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ ID NO:46;

(f) the polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ ID NO:2;

(g) the polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ ID NO:46;

(h) the polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ ID NO:2; and

(i) the polypeptide comprising amino acid number 1 (Met) to 649 (Ile) of SEQ ID NO:46, and

wherein the binding of the antibody to the isolated polypeptide is measured by a biological or biochemical assay including radioimmunoassay, radioimmuno-precipitation, Western blot, or enzyme-linked immunosorbent assay.

6. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment encoding a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 732 (Val) or an amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to 649 (Ile); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

7. An expression vector according to claim 6, further comprising a secretory signal sequence operably linked to the DNA segment.

8. A cultured cell comprising an expression vector according to claim 7, wherein the cell expresses a polypeptide encoded by the DNA segment.

9. An expression vector according to claim 6, wherein the DNA segment encodes a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 227 (Pro); or as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 519 (Glu); and

a transcription terminator,

wherein the promoter, DNA segment, and terminator are operably linked.

10. An expression vector according to claim 9, further comprising a secretory signal sequence operably linked to the DNA segment.

11. An expression vector according to claim 9, wherein the polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

12. An expression vector according to claim 9 wherein the polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2, or residues 544 (Lys) to 649 (Ile) of SEQ ID NO:46.

13. A cultured cell into which has been introduced an expression vector according to claim 9, wherein the cell expresses a soluble receptor polypeptide encoded by the DNA segment.

14. A DNA construct encoding a fusion protein, the DNA construct comprising:

a first DNA segment encoding a polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 19 (Ala);
- (b) the amino acid sequence of SEQ ID NO:54 from amino acid number 1 (Met), to amino acid number 32 (Ala);
- (c) the amino acid sequence of SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 227 (Pro);
- (d) the amino acid sequence of SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 519 (Glu);
- (e) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 520 (Ile) to amino acid number 543 (Leu);
- (g) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);
- (h) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);
- (i) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val); and
- (j) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile); and

at least one other DNA segment encoding an additional polypeptide,
wherein the first and other DNA segments are connected in-frame; and
wherein the first and other DNA segments encode the fusion protein.

15. An expression vector comprising the following operably linked elements:

a transcription promoter;
a DNA construct encoding a fusion protein according to claim 14; and
a transcription terminator,

wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

16. A cultured cell comprising an expression vector according to claim 15, wherein the cell expresses a polypeptide encoded by the DNA construct.

17. A method of producing a fusion protein comprising:
culturing a cell according to claim 16; and
isolating the polypeptide produced by the cell.

18. An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);

(e) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);

(f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val);

(g) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile);

(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 732 (Val); and

(i) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 1 (Met) to amino acid number 649 (Ile).

19. An isolated polypeptide according to claim 18, wherein the polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

20. An isolated polypeptide according to claim 18 wherein the polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2 or 544 (Lys) to 649 (Ile) of SEQ ID NO:46.

21. An isolated polynucleotide according to claim 18 wherein the polypeptide has activity as measured by cell proliferation, activation of transcription of a reporter gene, or wherein the polypeptide encoded by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids from the group consisting of:

(a) the polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ ID NO:2;

(b) the polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ ID NO:2;

(c) the polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ ID NO:2;

(d) the polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ ID NO:2;

(e) the polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ ID NO:46;

(f) the polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ ID NO:2;

(g) the polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ ID NO:46;

(h) the polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ ID NO:2; and

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(a) a polypeptide consisting of 9 to 713 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 732 (Val);

(b) a polypeptide consisting of 9 to 630 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:46 from amino acid number 20 (Ala), to amino acid number 649 (Ile);

(c) a polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ ID NO:2;

(d) a polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ ID NO:2;

(e) a polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ ID NO:2;

(f) a polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ ID NO:2;

(g) a polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ ID NO:46;

(h) a polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ ID NO:2;

(i) a polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ ID NO:46;

(j) a polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ ID NO:2;

(k) a polypeptide comprising amino acid number 1 (Met) to 649 (Ile) of SEQ ID NO:46,

(l) a polypeptide comprising amino acid residues 43 through 48 of SEQ ID NO:2;

(m) a polypeptide comprising amino acid residues 157 through 162 of SEQ ID NO:2;

(n) a polypeptide comprising amino acid residues 158 through 163 of SEQ ID NO:2;

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);

(e) the amino acid sequence as shown in SEQ ID NO:18;

the amino acid sequence as shown in SEQ ID NO:22; and

detecting the binding of the polypeptide to a ligand in the sample.

31. A method according to claim 30 wherein the polypeptide is membrane bound within a cultured cell, and the detecting step comprises measuring a biological response in the cultured cell.

32. A method according to claim 31 wherein the biological response is cell proliferation or activation of transcription of a reporter gene.